REMARKS/ARGUMENTS

Reconsideration and allowance of the above-referenced application are respectfully requested.

Revised Information Disclosure Statements are submitted herewith for the Examiner's consideration. The inadvertent errors appearing in the January 7, 2003 and May 12, 2003 Information Disclosure Statements are regretted.

Further, it is submitted that the objections to various claims, noted on page 4 of the Office Action, have been addressed by the amendments shown above and should be withdrawn accordingly.

Also, support for the 70% amino acid sequence identity recitation in claim 36 may be found, for example, on page 13, line 30 of the specification. Additionally, support for the 70% nucleotide sequence identity recitation may be found, for example, on page 13, line 30 of the specification. Support for the amendment relating to the amino acid sequence of the third histidine box of claim 36 may be found, for example, on page 53, line 21 of the specification.

Provisional Rejection of Claims 2-5 and 11-16 Under the Doctrine of Obviousness-Type Double Patenting

The Examiner has rejected claims 2-5 and 11-16 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 10, 16, 17 and 20 of copending Application No. 10/431,952.

It is requested that the rejection be held in abeyance until such time as allowable subject matter is noted by the Examiner in either application.

Rejection of Claims 2-5 Under 35 U.S.C. 112, First Paragraph

The Examiner has rejected claims 2-5 under Section 112, first paragraph, as failing to comply with the written description requirement. In particular, the Examiner alleges that the claims broadly encompass a genus of any nucleic acid molecule having 50% identity to the disclosed SEQ ID NO:13, wherein the sequence might or might not encode a functional desaturase or be derived from *S. diclina*.

In response, Applicants respectfully traverse the Section 112, first paragraph rejection. Structure and function has been correlated in delta-6-desaturases discovered to date. It is therefore submitted that the claims of the present invention meet the written description requirement in connection with sequences other than SEQ ID NO:13. More specifically, Applicants assert that all known membrane-bound desaturases, which include Δ6-, Δ5-, Δ4-, Δ9-, Δ12- and omega-3-desaturases, have a conserved motif composed of three histidine boxes (Histidine-boxes) (Pereira et al., Prostaglandins Leukot Essent Fatty Acids (2):97-106 (2003)):

Box 1: $HX_{(3-4)}H$

Box 2: $HX_{(2-3)}HH$

Box 3: $HX_{(2-3)}HH$

In these membrane bound desaturases, the histidine-boxes are separated by defined spacing within the sequence ($HX_{(3-4)}HX_{(7-41)}HX_{(2-3)}HHX_{(61-189)}HX_{(2-3)}HH$) (Pereira et al., *supra* (2003)). The three histidine-boxes (see over-lined residues of attached Figure 1) can be used to identify putative membrane-bound desaturases (Laoteng et al.,

Biochem Biophys Res Commun. 279(1):17-22 (2000); Pereira et al.,. Biochem J., 378(Pt 2):665-71 (2004); Qiu et al., J Biol Chem. 276(34):31561-6 (2001); and Zhang et al., FEBS Lett. 556(1-3):81-5 (2004))and were also used to identify the *S. diclina* Δ6-desaturase described in the current patent application (see Example 1; see also page 53, lines 12-21 of the specification). Conserved identical residues present in all Δ6-desaturases are indicated by '*' in attached Figure 1, and residues that are conserved in most Δ6-desaturases are indicated by ':' in attached Figure 1. The conservation of these residues across Δ6-desaturases of various origins (fungi to mammals) indicates their critical importance in the catalytic activity and structure of the desaturases. This has been demonstrated by site-directed mutagenesis studies with the membrane-bound rat Δ9-desaturase and the *Synechocystis* Δ12-desaturase (Shanklin et al., Biochemistry 33(43):12787-94 (1994) and Avelange-Macherel et al., FEBS Lett. 361(1):111-4 (1995)). Deletion of the conserved histidine residues within the histidine-boxes resulted in complete loss of enzymatic activity of the desaturases indicating that each of these histidine residues is essential for enzymatic activity (see Shanklin et al., supra (1994) and Avelange-Macheral, *supra* (1995)).

In all 'front-end' desaturases like the Δ6-, Δ5-, and Δ4-desaturases, the first histidine residue of the third histidine-box motif is replaced by a glutamine (i.e., $QX_{(2-3)}HH$ instead of $HX_{(2-3)}HH$) (Pereira et al., Prostaglandins Leukot Essent Fatty Acids (2):97-106 (2003)). This variant glutamine in the third histidine box of these 'front-end' desaturases is essential for catalytic activity as demonstrated by site-directed mutagenesis studies using the

Borage-Δ6 desaturase (Sayanova et al., Plant Physiol. 121(2):641-6 (1999)). In particular, replacing the variant glutamine residue by a histidine residue resulted in total loss of enzymatic activity of this Δ6-desaturase (Sayanova et al., supra (1999)).

In addition to the conserved histidine-boxes, the regions around each of the three histidine-boxes contain additional conserved residues indicating their importance in enzyme functionality. These sequences are (conserved residues indicated in bold):

His-Box 1 conserved region: QXGWXXHXXXH

His-Box 2 conserved region: GXSXXWWXXXHXXHHXXXNX$_{(4-11)}$DXD

His-Box 3 conserved region: QX$_{(14-19)}$WXXGGLXXQXXHHXFPXXPR

These regions are also conserved in the *S. diclina* Δ6-desaturase sequence claimed (see attached Figure 1).

The sequence that shares the highest overall percent nucleotide sequence identity (68.9% identity) with the *S. diclina* Δ6-desaturase is the Δ6-desaturase from *Pythium irregulare* (see attached Figure 2), as determined by GAP analysis (GCG-Wisconsin Package, Madison, WI). Further, the sequence the shares the highest overall percent amino acid sequence identity (59% identity) with the *S. diclina* Δ6-desaturase is the Δ6-desaturase from *Pythium irregulare* (see attached Figure 3), as determined by Blast analysis of the *S. diclina* Δ6-desaturase sequence with all sequences present in the public domain (NCBI).

The percent amino acid sequence identities of the *S. diclina* delta-6-desaturase with some of the known delta-6-desaturases are shown in attached Table I. The GenBank accession numbers of the delta-6-desaturases are listed in attached Table II. The *S. diclina* delta-6-desaturase has

greater percent identities with delta-6-desaturases from fungi than with those from mammals (see Table I).

Based upon the above, it can be concluded that a membrane-bound desaturase, encoded by a nucleic acid sequence of the present invention, must have three histidine-boxes along with their conserved region, as well as a histidine→glutamine variation in the third histidine-box, and it must demonstrate desaturase activity by inserting a double bond at carbon atom #6 of a fatty acid chain. Thus, there is a definite structure (i.e., conserved histidine-boxes)/function (i.e., the ability to desaturate a fatty acid) correlation in the case of Δ6-desaturases, thereby supporting the 70% recitation, written description requirement and scope of claims 2-5 and 36, for example. In particular, there are only a limited number of nucleic acid sequences that encode a desaturase having the properties recited in claims 2-5 and 36, for example. Therefore, in view of the references presented, that which is currently known in the art, and alignment data presented above, the subject matter of claims 2-5 is fully supported and satisfies the written description requirement. Thus, it is respectfully requested that the rejection be withdrawn.

Rejection of Claims 2-5 Under 35 U.S.C. 112, First Paragraph

The Examiner has rejected claims 2-5 under Section 112, first paragraph. In particular, the Examiner contends that the specification, while being enabling for an isolated nucleic acid comprising SEQ ID NO:13 or a nucleic acid encoding SEQ ID NO:14. wherein said nucleic acid

encodes a functionally active delta-6-desaturase, does not reasonably provide enablement for any nucleic acid comprising or complementary to at least about 50% of the nucleotide sequence set forth as SEQ ID NO:13.

Applicants respectfully traverse the rejection of claims 2-5 under Section 112, first paragraph. As argued above, based upon the knowledge of one of ordinary skill in the art, information present in the specification (see e.g., Example 2) and the relationship determined between structure and function in connection with delta-6-desaturases from other species, claims 2-5 are fully enabled. Thus, the rejection should be withdrawn. Undue experimentation would not be required in order to practice the claimed invention.

Rejection of Claims 11 and 13 Under 35 U.S.C. 112, First Paragraph

The Examiner has rejected claims 11 and 13 under Section 112, first paragraph. In particular, the Examiner alleges that the specification, while being enabling for a method of producing a desaturase in a host cell *in vitro* and an isolated host cell comprising a vector comprising the nucleic acid of SEQ ID NO:13, does not reasonable provide enablement for the method of host cell *in vivo*.

In response, Applicants respectfully traverse the rejection of claims 11 and 13 under Section 112, first paragraph. In particular, it is submitted that prior to the January 22, 2002 filing date of the present application and, more specifically, prior to the January 25, 2001 priority date of the presently claimed invention, one of ordinary skill in the art certainly would have known how to take the nucleic acid sequence corresponding to the

desaturase and introduce it into a plant or mammalian cell in order to produce the desired protein (see e.g., col. 14, line 35 - col. 18, line 13 of U.S. Patent No. 6,136,574; see also U.S. Patent No. 5,552,306, International Appln. Publication No. WO 94/11516 and International Appln. Publication No. 93/11245). Public information regarding the transformation of the host cell and its use in the production of a desaturase was known prior to the priority date of the present application.

In view of the above, it is submitted that the Section 112, first paragraph rejection of claims 11 and 13 has been overcome and should be withdrawn accordingly. The claims are fully enabled by the specification as well as that which was known in the art prior to the priority date of the present application.

Rejection of Claim 11 Under 35 U.S.C. 112, First Paragraph

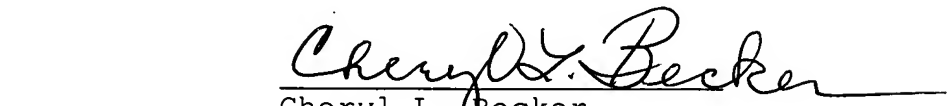
The Examiner has rejected claim 11 under Section 112, first paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner is concerned about the phrase "derived from".

In response, it is submitted that the amendment to claim 11 shown above adequately addresses the Examiner's concerns giving rise to the rejection. Thus, it is respectfully submitted that the rejection be withdrawn.

In conclusion, it is submitted that the subject application is in condition of allowance and Notice to that effect is respectfully requested.

Further, should the Examiner have any questions relating to the above, he is respectfully requested to contact the undersigned at the telephone number listed below.

Respectfully submitted,



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